B4 concld

12. (Amended) A pharmaceutical composition comprising a sulfated polysaccharide as in any one of claims 1 to 7.

B5

14. (Twice Amended) A method of treatment of medical conditions mediated by a matrix metalloproteinase wherein the treatment comprises applying to a wound the sulfated polysaccharide of claim 1.

REMARKS

The Examiner is thanked for withdrawing the Final Rejection of March 9, 2001. Amendments to claims 11, 12, and 14 where made to overcome the Examiner's objections under 37 C.F.R 1.75(c) or second paragraph of 35 U.S.C 112. Reconsideration is respectfully requested to consider claim 16 as part of the examination as the burden on applicant for having to file, prosecute, and eventually maintain a second patent outweighs the additional searching, if any at all, that would be required to have claim 16 examined with the currently pending claims. Support for amendments to claims 1-11 may be found in the Specification, for example, on page five, lines 15-26 and page 6, lines 4-8.

By way of review, it has been found surprisingly, that the sulfated polysaccharides according to the present invention have an exceptional ability to bind to matrix metallproteinases (MMP's). Such matrix metalloproteinases are implicated in a number of medical conditions,

including chronic wounds such as decubitis ulcers. This is because the balance between matrix deposition and tissue turnover, which in turn may depend on the balance between proteolytic enzymes and their inhibitors, is fundamental to wound healing and other medical conditions. Chronic wound fluids have been shown to contain elevated levels of MMP2 (Gelatinase A) and MMP9 (Gelatinase B).

Also it has been found, surprisingly, that the sulfated polysaccharides according to the present invention has anticoagulant properties. Such properties are the exact opposite of the haemostatic properties well known for ORC itself. Accordingly, the present invention further provides the use of a sulfated polysaccharides according to the present invention for the preparation of the an anticoagulant medicinal composition.

§103

A. Claims 1-10 were rejected under §103(a) as unpatentable over US 3,709,877 (Tunc). This rejection is respectfully traversed.

Tunc discloses sulfated cellulose esters used as binders in nonwoven fabrics.

As amended claims 1-10 are directed to wound dressings or ointments wherein the wound dressing or ointment comprises an effective amount of a synthetic sulfated polysaccharide to bind MMP's.

From Tunc it is not apparent why the claimed wound dressings or ointment which bind MMP's would be obvious. More specifically Tunc is silent with regard to the claimed wound dressing or ointment, but more importantly Applicants have demonstrated that the sulfated polysaccharides of the present invention are superior in binding MMP which have been implicated in preventing the healing of chronic wounds (See included article "Wound Fluid from Chronic Leg Ulcers Contains Elevated Levels of Metalloproteinases MMP-2 and MMP-9" by Wysocki et al; please note distinction between "chronic" wounds and "acute" wounds.). Since Tunc is not concerned with treatment of chronic wounds and binding of MMP's, Applicants submit this rejection is improper and respectfully request its withdrawal.

B. Claims 1-10 were rejected under §103(a) as unpatentable over EP 140,596 (Easton) in view of Tunc. This rejection is respectfully traversed.

Easton is directed to complexes of polyanionic plant polysaccharides with biodegradable proteins or proteolytic degradation products thereof and are useful in the formation of wound dressings and surgical implants, such as sutures, blood vessel grafts and artificial organs. The biodegradable protein part of the complex is preferably collagen.

Applicants incorporate by reference this traversal provided in view of Tunc. Applicants respectfully submit that Easton adds nothing further to the Examiner's arguments. More noteworthy

is the fact that Easton, while disclosing various forms of polysaccharides, contains no indication that the sulfated polysaccharides of the present invention are superior to other non-sulfated polysaccharides in binding MMP's as demonstrated by Applicant's comparative data (Please note Fig. 1 and accompanying discussion on the superiority of sulfated polysaccharides in binding MMP's). Therefore, this rejection is respectfully requested to be withdrawn.

C. Claims 1-10, 14 and 15 were rejected under §103(a) as unpatentable in view of US 5,679,375 (Spilburg). This rejection is respectively traversed.

Spilburg is concerned with a composition for treating gastric or duodenal ulcers using sulfated polysaccharides which are non-absorbable in the gastro-intestinal tract. (claim 1 and column 2, lines 45-54.)

Applicants submit that it is not obvious to use something for internal bodily treatment of gastric ulcers for topical wound dressing or ointment applications and methods to bind MMP's present in chronic wounds. Please note that gastric ulcers are quite different from chronic ulcers; i.e. proteases found in the chronic ulcer environment compared to proteases found in the gastric environment are quite different. For example, proteases found in gastric ulcers are acidic (pH $\simeq$2) and therefore are only active at low pH. However, in the case of chronic ulcers, the pH of the ulcer is approximately 7, and the MMP's found in the chronic wounds are only active in the pH range of about 6-8. Thus, due to the widely different applications and environments between those disclosed in Spilburg and those of Applicant's invention, it is respectfully submitted that this rejection is improper and Applicants, therefore, respectfully request its withdrawal.

Based on the foregoing, Applicant believes the application is now in condition for allowance. Favorable reconsideration and early notice of allowance are earnestly solicited. The Commissioner is authorized to charge Deposit Account No. 10-0750/JJM-399/TJS any additional fees which may be required. If any questions arise which can be disposed through interview, the Examiner is encouraged to contact Applicants' attorney at the telephone number listed below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

1. (Twice amended) A wound dressing or ointment comprising a synthetic sulfated polysaccharide selected from the group consisting of sulfated cellulose derivatives and sulfated polyanioninc polysaccharides, said synthetic sulfated polysaccharide being present in an amount sufficient to bind matrix metalloproteinases.

2. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1, selected from the group consisting of sulfated hydroxyethyl cellulose, sulfated carboxymethyl cellulose and sulfated oxidized regenerated cellulose.

3. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1 which is sulfated oxidized regenerated cellulose.

4. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1, selected from the group consisting of sulfated alginates, sulfated pectins and sulfated hyaluronic acid.

5. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1 which is a sulfated alginate.

6. (Twice Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to any preceding claim, comprising an average of at least 0.1 sulfate groups for each saccharine residue of the polysaccharide.

7. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 6, comprising an average of at least 1 sulfate group for each saccharine residue of the polysaccharide.

8. (Twice Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1 having an average molecular weight in the range 25,000 - 250,000.

9. (Twice Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1 in the form of a woven, non-woven, sponge or knitted fabric.

10. (Twice Amended) A wound dressing or ointment comprising the sulfated polysaccharide according to claim 1 in the form of a solid complex with collagen.

11. (Amended) A wound dressing or ointment comprising the sulfated polysaccharide ~~according to any~~ as in any one of claims 1 to 7 which is soluble in water to an extent of at least 10g/l at 25^{O}C.

12. (Amended) A pharmaceutical composition comprising a sulfated polysaccharide ~~according to any~~ as in any one of claims 1 to ~~12~~ 7.

14. (Twice Amended) A method of treatment of medical conditions mediated by a matrix metalloproteinase wherein the treatment comprises applying to a wound the ~~composition~~ sulfated polysaccharide of claim 1.